PhD in Pharmacy

Research Area: Pharmaceutical Biotechnology

Title: Characterization of the effect of APOBEC3 proteins on HIV-2 infection: Contribution to development of new therapies.

At present, it is believed that the best (only) way to prevent the spread of HIV infection is by a vaccine. However, the lack of knowledge in the functioning of the immune system in general and in particularly on the immune response to HIV infection has not allowed the development of an effective one. Thus, the current treatment for controlling HIV infection consists of a cocktail of drugs that inhibit the operation of various viral proteins, but this have several side effects and led to the emergence of (a) resistant virus, making very important the discover of new drugs. Viral infectivity factors (Vif proteins) are promising targets for a new antiviral strategy, since they are essential for viral replication in vivo. Their primary function is to neutralize the anti-retroviral cellular factor APOBEC3G, which is normally expressed in natural HIV target cells. However, our previously work have shown that viral inhibition by APOBEC3G is much less effective against HIV-2 than HIV-1. Besides, it is know that the pathogenic potential of HIV-1 and HIV-2 are very different. HIV-2 generally progresses more slowly than HIV-1 and the HIV-2-infected individuals survive as long-term non-progressors. These infectivity differences may be related to the Vif2/APOBEC3 interactions. Since, HIV-2 is much less studied than HIV-1 and generally it is assumed that these two types of viruses have the same molecular mechanisms of action, the initial purpose of this study is to clarify the duality between viral and host antiviral factors in HIV-2 infection with focus in Vif-2 and antiviral effects of several members of the APOBEC3 protein family. As next step, the study also aims to use the knowledge obtained to develop a new strategy based in lentiviral vectors for gene therapy in HIV infections or in others pathologies where APOBEC3 proteins are knowned to have a crucial role. Thus, this study will help to broaden the knowledge on innate cellular immunity protective of the host, and will contribute to explain the differences between HIV-2 and HIV-1 infectivity. This knowledge is essential for designing new anti-viral drugs using Vif as a target and also contributes to the development of new therapies for other diseases, like cancer.

Keywords: APOBEC 3 proteins, HIV-2 infectivity, molecular mechanisms, gene therapy

Publications

https://doi: 10.1093/mutage/get052

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https://doi: 10.1080/07853890.2018.1427445

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